ON THE SOLVABILITY OF A MATHEMATICAL MODEL FOR PRION PROLIFERATION

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Abstract. We show that a model describing the interaction between normal and infectious prion proteins admits global solutions. More precisely, supposing the involved degradation rates to be bounded, we prove global existence and uniqueness of classical solutions. Based on this existence theory, we provide sufficient conditions for the existence of global weak solutions in the case of unbounded splitting rates. Moreover, we prove global stability of the disease free steady state.

1. Introduction

The present paper aims at investigating mathematically a recent model that describes the dynamics of prion proliferation. Prions seem to be widely regarded as the infectious agent causing fatal diseases known as bovine spongiform encephalopathy (BSE) for cattle, scrapie for sheep, or Kuru and Creutzfeld-Jacob for humans. In this theory, prions are thought to be a polymeric form of a normal protein monomer $\text{PrP}^C$. The polymeric infectious prions $\text{PrP}^{Sc}$ have a tendency to attach units of $\text{PrP}^C$ in a stringlike formation, converting the latter to the infectious form. This mechanism makes $\text{PrP}^{Sc}$ polymers more stable and is called nucleated polymerization. Above some critical size, $\text{PrP}^{Sc}$ is very stable and polymerizes rapidly to form chains, possibly involving several thousands of monomer units. Nevertheless, $\text{PrP}^{Sc}$ prions also can split, usually into smaller infectious prions. However, if a polymer falls below the critical size, it degrades immediately into $\text{PrP}^C$ monomers. A model for nucleated polymerization has recently been proposed in [3], [4] (see also the references therein) describing the mechanism by which prions are hypothesized to replicate. Denoting the number of $\text{PrP}^C$ monomers at time $t \geq 0$ by $v(t) \geq 0$ and introducing a population density $u = u(t, y) \geq 0$ for the infectious $\text{PrP}^{Sc}$ polymers at time $t \geq 0$ and size $y$ greater than the minimum length $y_0 > 0$, the interaction of the $\text{PrP}^C$ monomers and the $\text{PrP}^{Sc}$ polymers can be described by the coupled system consisting of the ordinary differential equation

$$\dot{v} = \lambda - \gamma v - \tau v \int_{y_0}^{\infty} u(t, y) \, dy + 2 \int_{y_0}^{\infty} u(t, y) \beta(y) \int_{0}^{y_0} y' \kappa(y', y) \, dy' \, dy$$  \hspace{1cm} (1)

and the partial differential equation

$$\partial_t u + \tau v(t) \partial_y u = -(\mu(y) + \beta(y))u(y) + 2 \int_{y}^{\infty} \beta(y') \kappa(y, y') u(y') \, dy'$$  \hspace{1cm} (2)

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for \( y \in (y_0, \infty) \) subject to the boundary condition
\[
 u(t, y_0) = 0 , \quad t > 0 .
\] (3)
These equations are supplemented with the initial conditions
\[
 v(0) = v^0 , \quad u(0, y) = u^0(y) , \quad y \in (y_0, \infty) .
\] (4)
Equation (1) includes a source term \( \lambda \geq 0 \), while the term \( -\gamma v(t) \), with \( \gamma \geq 0 \), takes into account metabolic degradation of monomers. The constant \( \tau > 0 \) denotes the polymerization rate. Moreover, \( \beta(y) \geq 0 \) is the length-dependent fragmentation rate of polymers of size \( y > y_0 \), and \( \kappa(y', y) \) is the probability of a polymer of size \( y > y_0 \) splitting into two pieces \( y' < y \) and \( y - y' < y \). The transport term \( \tau v(t) \partial_y u(t, y) \) in equation (2) accounts for the loss of polymers of size \( y \) due to lengthening. A loss of polymers according to metabolic degradation is reflected by the term \( -\mu(y) u(y) \). Finally, the terms involving \( \beta \) on the right hand side of equation (2) represent the loss and gain of PrPSc polymers caused by splitting. For a more detailed explanation of each process we refer to [3], [4] and the references therein.

Let us point out that (1), (2) is a coupled system of non-linear, non-local equations. In order to solve this equations we employ Kato’s theory for hyperbolic evolution equations. That is, given a function \( v \) with appropriate regularity properties, we construct an evolution system for the partial differential equation (2). We should remark that in the absence of the kernel operator on the right hand side of (2), an evolution system can readily be obtained by using the method of characteristics.

It should also be pointed out that equations (1), (2) can be handled as an abstract quasilinear hyperbolic system in order to obtain local existence, see for instance [7, §6.4]. However, this approach does not seem to yield optimal results for equations (1), (2).

Before outlining the contents of this paper, we summarize the present-state of knowledge on the above model. It seems that merely kernels of the form
\[
 \mu \equiv \text{const} , \quad \beta(y) = \beta y , \quad \kappa(y', y) = \frac{1}{y}
\] (5)
have been considered so far. This choice of kernels leads to a closed system of ordinary differential equations for \( v \) and
\[
 U(t) := \int_{y_0}^{\infty} u(t, y) \, dy , \quad P(t) := \int_{y_0}^{\infty} y u(t, y) \, dy .
\]
Indeed, (1) reduces to
\[
 \dot{v} = \lambda - \gamma v - \tau v U + \beta y_0^2 U ,
\] (6)
and integrating (2) yields the equations
\[
 \dot{U} = \beta P - \mu U - 2 \beta y_0 U ,
\] (7)
\[
 \dot{P} = \tau v U - \mu P - \beta y_0^2 U ,
\] (8)
which, together with (6), are uniquely globally solvable. In addition, it has been shown in [4] that the disease free steady state \((v,U,P) = (\lambda/\gamma,0,0)\) for the equations (6)-(8) is globally stable provided

\[ \beta y_0 + \mu > \sqrt{\frac{\beta \lambda \tau}{\gamma}}. \] (9)

If one reverses the strict inequality sign in (9) it has also been proved in [4] that there exists a prion disease steady state which is locally asymptotically stable. The latter result has been improved in [9] to global stability.

Observe that the solvability of (6)-(8) implies that the original equations (1), (2) are no longer coupled since \(v\) is completely determined for all \(t \geq 0\). Hence, as shown in [8], the partial differential equation (2) (with kernels as in (5)) can be solved for \(u = u(t,y)\) by using the method of characteristics combined with semigroup theory. Moreover, it has also been shown in [8] that \(u\) converges either to 0 or to the disease steady state according to whether or not (9) holds.

Our aim is to consider quite general kernels, merely assuming suitable growth conditions. More precisely, after collecting some auxiliary results in section 2, we show in section 3 that (1)-(4) is globally well-posed provided \(\mu\) and \(\beta\) are bounded, see Theorem 3.1. The basic idea is to solve equation (1) for a fixed, suitable function \(\bar{u}\) and then to substitute the obtained solution \(\bar{v}\) into equation (2). Using Kato’s theory for hyperbolic evolution equations, we solve then equation (2) in order to obtain a classical solution \(u_{\bar{u}}\). A fixed point argument for the map \(\bar{u} \mapsto u_{\bar{u}}\) yields then local existence and uniqueness of a solution pair \((v,u)\) for (1)-(4). Suitable a priori estimates guarantee global existence. A weak formulation of (2) allows then to extend in section 4 the existence results to unbounded kernels by using a weak compactness method, see Theorem 4.3. We also prove finite speed of propagation for the weak (and classical) solutions to (2). Finally, in section 5 we show that the disease free steady state is globally asymptotically stable provided some suitable lower and upper bounds for the splitting kernels are available. We refer to Theorem 5.2 for a precise statement.

Clearly, the method described above does not yield uniqueness of weak solutions. This issue will be the topic of future work.

2. Preliminaries

In the following, we set \(Y := (y_0,\infty)\) and assume that

\[ \mu, \beta \in L^+_\infty(Y), \] (10)

where \(L^+_\infty(Y)\) stands for the positive cone in \(L_\infty(Y)\). We also assume that \(\kappa \geq 0\) is measurable on \(K := \{(y',y); y_0 < y < \infty, 0 < y' < y\}\) and satisfies

\[ \kappa(y',y) = \kappa(y-y',y), \quad (y',y) \in K, \] (11)

which means binary splitting. Moreover, we suppose the number of monomer units to be preserved during splitting, that is,

\[ 2 \int_0^y y' \kappa(y',y) dy' = y, \quad \text{a.e. } y \in Y. \] (12)
Furthermore, we let
\[ \tau > 0, \quad \lambda, \gamma \geq 0. \quad (13) \]
It is easy to check that (10)-(12) imply
\[ \int_0^y \kappa(y', y) \, dy' = 1, \quad \text{a.e. } y \in Y, \quad (14) \]
and that the operator \( L \), given by
\[ L[u](y) := - (\mu(y) + \beta(y)) u(y) + 2 \int_y^\infty \beta(y') \kappa(y, y') u(y') \, dy', \quad \text{a.e. } y \in Y, \quad (15) \]
defines a linear and bounded operator from \( L_1(Y, y \, dy) \) into itself. Also note that
\[ \int_{y_0}^\infty \varphi(y) L[u](y) \, dy = - \int_{y_0}^\infty \varphi(y) \mu(y) u(y) \, dy + \int_{y_0}^\infty u(y) \beta(y) \left( - \varphi(y) + 2 \int_{y_0}^y \varphi(y') \kappa(y', y') \, dy' \right) \, dy \quad (16) \]
for \( u \in L_1(Y, y \, dy) \) and a suitable test function \( \varphi \). We then put
\[ E_0 := L_1(Y, y \, dy) \quad \text{and} \quad E_1 := \dot{W}^1_1(Y, y \, dy) := \text{cl}_{W^1_1(Y, y \, dy)} \mathcal{D}(Y), \]
where \( \mathcal{D}(Y) \) denotes the space of all test functions on \( Y \). By \( E^+_0 \) we mean the positive cone in \( E_0 \) and \( E^+_1 := E_1 \cap E^+_0 \). Finally, given any interval \( J \) and any function \( v : J \to \mathbb{R}^+ \), we define
\[ A_v(t) u := \tau v(t) \partial_y u - L[u], \quad u \in E_1, \quad t \in J. \quad (17) \]

**Lemma 2.1.** The operator \(-A\), defined as
\[ A \varphi := \partial_y \varphi, \quad \varphi \in E_1, \quad (18) \]
generates a strongly continuous semigroup \( \{ e^{-tA} ; t \geq 0 \} \) on \( E_0 \). It is given by
\[ [e^{-tA} \varphi](y) = \begin{cases} \varphi(y-t), & y > y_0 + t, \\ 0, & y_0 < y \leq y_0 + t, \end{cases} \quad t \geq 0, \quad (19) \]
and satisfies
\[ \| e^{-tA} \varphi \|_{L(E_0)} \leq e^{t/y_0}, \quad t \geq 0. \quad (20) \]

**Proof.** Clearly, (19) defines a strongly continuous semigroup on \( E_0 \) satisfying
\[ \| e^{-tA} \varphi \|_{E_0} \leq \left( 1 + \frac{t}{y_0} \right) \| \varphi \|_{E_0} \leq e^{t/y_0} \| \varphi \|_{E_0}, \quad t \geq 0, \]
for \( \varphi \in E_0 \), whence (20). It thus remains to show that its generator \(-A\) is indeed given by (18). Note that Lebesgue’s theorem guarantees that the test functions are contained in the domain of \( A \) and that
\[ A \varphi = \partial_y \varphi, \quad \varphi \in \mathcal{D}(Y). \quad (21) \]
Since (19) is a right translation, \( \mathcal{D}(Y) \) is invariant under \( e^{-tA} \) and therefore is a core for \( A \). In particular, \( \mathcal{D}(Y) \) is dense in the domain of \( A \), which, together with (21), easily yields (18). \( \square \)
In the sequel, we set $J_T := [0, T]$ for $T > 0$ and, given $R > 1$, we define

$$\mathcal{V}_{T,R} := \{ v \in C^1(J_T); R^{-1} \leq v(t) \leq \|v\|_{C^1(J_T)} \leq R \}.$$  \hfill (22)

Recall then that the operator $A_v(t)$ has been defined in (17).

**Proposition 2.2.** Fix $R > 1$, $T_0 > 0$ and let $0 < T \leq T_0$. Then $(-A_v(t))_{t \in [0,T]}$ generates for each $v \in \mathcal{V}_{T,R}$ a unique evolution system $U_v(t,s)$, $0 \leq s \leq t \leq T$, in $E_0$, and there exists a constant $\omega_0 := \omega_0(T_0, R) > 0$ such that

$$\|U_v(t,s)\|_{\mathcal{L}(E_0)} \leq e^{\omega_0(t-s)}, \quad 0 \leq s \leq t \leq T, \quad v \in \mathcal{V}_{T,R},$$  \hfill (23)

and

$$\|U_v(t,s)\|_{\mathcal{L}(E_1)} \leq \omega_0, \quad 0 \leq s \leq t \leq T, \quad v \in \mathcal{V}_{T,R}.$$  \hfill (24)

Moreover, for $v, w \in \mathcal{V}_{T,R}$, it holds that

$$\|U_v(t,s) - U_w(t,s)\|_{\mathcal{L}(E_0)} \leq \omega_0 (t-s) \|v-w\|_{C(J_T)}, \quad 0 \leq s \leq t \leq T.$$  \hfill (25)

**Proof.** Since $L$ is a bounded operator on $E_0$, Lemma 2.1 and a well-known perturbation result (see [7, Thm.3.1.1]) ensure that, for any fixed $v \in \mathcal{V}_{T,R}$ and any $s \in J_T$, $-A_v(s)$ generates a strongly continuous semigroup on $E_0$ with

$$\|e^{-\bar{\omega}_v(s)}\|_{\mathcal{L}(E_0)} \leq e^{\bar{\omega} t}, \quad t \geq 0,$$  \hfill (26)

where $\bar{\omega} := \tau R \omega_0^{-1} + \|L\|_{\mathcal{L}(E_0)}$. Hence, putting $\omega := \bar{\omega} + 1$ it follows that $\{A_v(t)\}_{t \in J_T}$ is stable in the sense of [7, §5.2] for each $v \in \mathcal{V}_{T,R}$. Next, given any $t \in J_T$, the definition $Q_v(t) := \omega + A_v(t)$ yields an isomorphism from $E_1$ onto $E_0$ satisfying

$$\|Q_v(t)\|_{\mathcal{L}(E_1, E_0)} \leq \omega + \tau R + \|L\|_{\mathcal{L}(E_0)}, \quad t \in J_T, \quad v \in \mathcal{V}_{T,R}.$$  \hfill (27)

Moreover, for $u \in E_1$, $Q_v(\cdot)u \in C^1(J_T, E_0)$ with $\dot{Q}_v(t)u := \frac{d}{dr}Q_v(t)u = \tau \dot{v}(t)\partial_yu$.

Therefore, assumptions $(H_1), (H_2)^+, (H_3)$ of [7, §5] hold, thus implying that there indeed exists a unique evolution system $U_v(t,s)$, $0 \leq s \leq t \leq T$, in $E_0$ for each $v \in \mathcal{V}_{T,R}$, which, in addition, satisfies statements (E1)–(E5) of [7, §5]. In particular, (23) holds (with $\omega$ replaced by $\bar{\omega}$).

We now refer to the proof of [7, Thm.5.4.6]: The evolution system $U_v(t,s)$ can be written as

$$U_v(t,s) = Q_v(t)^{-1}W_v(t,s)Q_v(s), \quad 0 \leq s \leq t \leq T,$$  \hfill (28)

where $W_v(t,s) \in \mathcal{L}(E_0)$ satisfies

$$W_v(t,s)u = U_v(t,s)u + \int_s^t W_v(t,r)C_v(r)U_v(r,s)u \, dr$$

for $0 \leq s \leq t \leq T$ and $u \in E_0$ with

$$C_v(t) := \dot{Q}_v(t)Q_v(t)^{-1} \in \mathcal{L}(E_0), \quad t \in J_T.$$  

We then claim that there is a constant $c_0(R) > 0$ such that

$$\|Q_v(t)^{-1}\|_{\mathcal{L}(E_0, E_1)} \leq c_0(R), \quad t \in J_T, \quad v \in \mathcal{V}_{T,R}.$$  \hfill (29)

Indeed, (26) implies

$$\|Q_v(t)^{-1}\|_{\mathcal{L}(E_0)} \leq 1, \quad t \in J_T,$$
and therefore, for $u \in E_0$ and $t \in J_T$, 
\[
\|Q_v(t)^{-1}u\|_{E_1} = \|Q_v(t)^{-1}u\|_{E_0} + \|\partial_y Q_v(t)^{-1}u\|_{E_0}
\leq \|u\|_{E_0} + \frac{1}{\tau v(t)} \|u - (\omega - L) Q_v(t)^{-1}u\|_{E_0}
\leq (1 + R/\tau (1 + \omega + \|L\|_{\mathcal{L}(E_0)})) \|u\|_{E_0},
\]
whence (29). Consequently, we have 
\[
\|C_v(t)\|_{\mathcal{L}(E_0)} \leq \|Q_v(t)\|_{\mathcal{L}(E_1, E_0)} \|Q_v(t)^{-1}\|_{\mathcal{L}(E_0, E_1)} 
\leq \tau \|\hat{v}\|_{\mathcal{L}(J_T)} e_0(R) \leq c_0(R)
\]
for $t \in J_T$ and $v \in \mathcal{V}_{T,R}$. From the proof of [7, Lem.5.4.5] (see in particular equation (4.11) therein) and from (23) it thus follows that there exists a constant 
$c(T_0, R) > 0$ such that 
\[
\|W_v(t, s)\|_{\mathcal{L}(E_0)} \leq c(T_0, R), \quad 0 \leq s \leq t \leq T, \quad v \in \mathcal{V}_{T,R}.
\]
Applying estimates (27), (29), and (30) to (28) we conclude that (24) is true.

Finally, let $v, w \in \mathcal{V}_{T,R}$ and $u \in E_1$ be arbitrary. Then, for $0 \leq s < t \leq T$, 
\[
N := [\sigma \mapsto U_v(t, \sigma) U_w(\sigma, s) u] \in C^1((s, t), E_0) \cap C([s, t], E_1)
\]
by $(E_2) - (E_5)$ in [7, §5] with 
\[
N(\sigma) = U_v(t, \sigma) (\hat{A}_v(\sigma) - \hat{A}_w(\sigma)) U_w(\sigma, s) u.
\]
Therefore, (23) and (24) yield 
\[
\|U_w(t, s)u - U_v(t, s)u\|_{E_0}
\leq \int_s^t \|U_v(t, \sigma)\|_{\mathcal{L}(E_0)} \|\hat{A}_v(\sigma) - \hat{A}_w(\sigma)\|_{\mathcal{L}(E_1, E_0)} \|U_w(\sigma, s)\|_{\mathcal{L}(E_1)} \, d\sigma \|u\|_{E_1}
\leq c(T_0, R) (t - s) \|v - w\|_{\mathcal{L}(J_T)} \|u\|_{E_1}
\]
for $0 \leq s \leq t \leq T$. Hence statement (25). \qed

**Remark 2.3.** As observed in the previous proof, the evolution system $U_v(t, s), 0 \leq s \leq t \leq T$, corresponding to $v \in \mathcal{V}_{T,R}$ satisfies $(E_3) - (E_5)$ in [7, §5]. In particular, we have for $u^0 \in E_1$ that 
\[
[t \mapsto U_v(t, 0) u^0] \in C^1(J_T, E_0) \cap C(J_T, E_1).
\]

The existence of weak solutions will require the following auxiliary result.

**Lemma 2.4.** For $v \in C(J_T)$ with $v(t) \geq 0$ put $A_v(t) := \tau v(t) \partial_y$, $t \in J_T$, and let 
$U_{A_v}(t, s), 0 \leq s \leq t \leq T$, be the corresponding evolution system in $L_1(Y)$. Then, 
for any $\delta > 0$, it holds that 
\[
\sup_{|E| \leq \delta} \int_E U_{A_v}(t, s) \varphi \, dy \leq \sup_{|E| \leq \delta} \int_E \varphi \, dy, \quad 0 \leq s \leq t \leq T, \quad \varphi \in L_1^+(Y),
\]
the supremum being taken over all measurable sets $E \subset Y$.

**Proof.** Noticing that $-\partial_y$ with domain $\hat{W}_1^1(Y)$ generates a strongly continuous positive semigroup of contractions on $L_1(Y)$ given as in (19), it follows that 
\[
\|e^{-tA_v(s)}\|_{\mathcal{L}(L_1(Y))} \leq 1, \quad \|e^{-tA_v(s)}\|_{\mathcal{L}(\hat{W}_1^1(Y))} \leq 1, \quad t \geq 0, \quad s \in J_T.
\]
Hence, the corresponding evolution system $U_{A_v}(t, s)$, $0 \leq s \leq t \leq T$, in $L_1(Y)$ is well-defined according to [7, Thm.5.2.2, Thm.5.3.1]. Let then $E \subset Y$ be any measurable subset of $Y$ with measure $|E| \leq \delta$ and choose $\varphi \in L_1^+(Y)$. Denoting by $\chi_S$ the characteristic function on a set $S$, we have

$$\int_E \left[ e^{-t A_v(s)} \varphi \right](y) \, dy = \int_{y_0}^{\infty} \chi_{t - t\varphi(s) + \varepsilon}(y) \varphi(y) \, dy \leq \sup_{|E'| \leq \delta} \int_{E'} \varphi(y) \, dy$$

for $s \in J_T$ and $t \geq 0$. From equations (3.5) and (3.15) in [7, §5] we thus deduce

$$\int_E U_{A_v}(t, s) \varphi \, dy \leq \sup_{|E'| \leq \delta} \int_{E'} \varphi \, dy, \quad 0 \leq s \leq t \leq T,$$

and the assertion follows.

\[ \square \]

3. Classical Solutions

In this section we show that problem (1)-(4) is globally well-posed for bounded kernels $\mu$ and $\beta$. In order to do this, let us denote by $| \cdot |$ the norm in $L_1(Y)$ and put

$$g(u) := 2 \int_{y_0}^{\infty} u(y) \beta(y) \int_0^{y_0} y' \kappa(y', y) \, dy' \, dy.$$ 

Defining $L$ by (15) and $A_v(t)$ by (17), we may rewrite (1)-(4) as

$$\dot{v} = \lambda - \gamma v - \tau v |u| + g(u), \quad t > 0, \quad v(0) = v^0,$$

(31)

provided $u \geq 0$, and

$$\dot{u} + A_v(u) = 0, \quad t > 0, \quad u(0) = u^0.$$ 

(32)

**Theorem 3.1.** Suppose (10)-(13) hold. Then, given any $v^0 > 0$ and $u^0 \in E_1^+$, problem (31), (32) possesses a unique global classical solution $(v, u)$ such that $v \in C^1(\mathbb{R}^+)$, $v(t) > 0$ for $t > 0$, and $u \in C^1(\mathbb{R}^+, E_0) \cap C(\mathbb{R}^+, E_1^+)$.

**Proof.** (i) We first prove that, for any $S > 0$, there exists $T := T(S) \in (0, 1]$ such that (31), (32) possesses a unique solution $(v, u)$ on $J_T$ with regularity properties as stated in the theorem, provided that $(v^0, u^0) \in \mathbb{R}^+ \times E_1^+$ satisfy

$$S^{-1} \leq v^0 \quad \text{and} \quad v^0 + \|u^0\|_{E_1^+} \leq S.$$ 

(33)

In the following, we denote by $c(S) > 0$ a generic constant depending on $S$ but not on $T \in (0, 1]$. Let us then define the complete metric space

$$X_T := \left\{ u \in C(J_T, E_0^+): \|u(t)\|_{E_0} \leq S + 1, \ t \in J_T \right\},$$

and let us choose $\bar{u} \in X_T$ arbitrarily. Then, since $g(\bar{u}), |\bar{u}|_1 \in C(J_T)$ due to (12), it follows that (31), with $u$ replaced by $\bar{u}$, admits a unique solution $v_{\bar{u}} \in C^1(J_T)$. Clearly,

$$v_{\bar{u}}(t) = e^{-\gamma t} \int_0^{t} |\bar{u}(s)|_1 \, ds \, v^0$$

$$+ \int_0^{t} e^{-\gamma (t-s)} \int_0^{s} |\bar{u}(\sigma)|_1 \, d\sigma \left( \lambda + g(\bar{u}(s)) \right) \, ds$$

for $t \in J_T$, hence

$$v_{\bar{u}}(t) \geq e^{-\gamma t/y_0(S+1)t} v^0 \geq c(S), \quad 0 \leq t \leq T \leq 1.$$ 

(34)
Moreover, since $v^0 \leq S$ and $g(\tilde{u}(t)) \leq \|\beta\|_\infty (S + 1)$ for $t \in J_T$, we deduce
\[ v_\tilde{u}(t) \leq c(S), \quad t \in J_T, \] (35)
from which it follows
\[ -c(S) \leq - (\gamma + \tau |\tilde{u}(t)|_1) v_\tilde{u}(t) \leq \dot{v}_\tilde{u}(t) \leq \lambda + g(\tilde{u}(t)) \leq c(S), \quad t \in J_T. \] (36)
Therefore, (34)-(36) entail the existence of $R := R(S) > 1$, depending on $S > 0$ but not on $T \in (0, 1]$, such that $v_\tilde{u} \in \mathcal{V}_{T,R}$ whenever $\tilde{u} \in X_T$, where $\mathcal{V}_{T,R}$ is given by (22). Furthermore, we readily derive from the explicit representation of $v_\tilde{u}$ and the linearity of $g$ that
\[ |v_{\tilde{u}_1}(t) - v_{\tilde{u}_2}(t)| \leq c(S) \|\tilde{u}_1 - \tilde{u}_2\|_{X_T}, \quad 0 \leq t \leq T \leq 1, \quad \tilde{u}_1, \tilde{u}_2 \in X_T. \] (37)
Let $U_{\tilde{u}_a}(t,s)$, $0 \leq s \leq t \leq T$, denote the unique evolution system in $E_0$ corresponding to $\{\tilde{A}_{\tilde{u}_a}(t)\}_{t \in J_T}$ and by $\omega_0 = \omega_0(1,R(S))$ the constant occurring in Proposition 2.2. Defining
\[ \Lambda(\tilde{u})(t) := U_{\tilde{u}_a}(t,0) u^0, \quad t \in J_T, \quad \tilde{u} \in X_T, \]
we obtain by Remark 2.3 the unique solution in $C(J_T,E_1) \cap C^1(J_T,E_0)$ to
\[ \dot{\tilde{u}} + \tilde{A}_{\tilde{u}_a}(t) u = 0, \quad t > 0, \quad u(0) = u^0. \]
Next we show that $\Lambda : X_T \to X_T$ is a contraction, which, consequently, would imply our first claim. Provided $T := T(S) \in (0,1]$ is chosen sufficiently small, we deduce from (23) that, for $\tilde{u} \in X_T$ and $t \in J_T$,
\[ \|\Lambda(\tilde{u})(t)\|_{E_0} \leq e^{\omega_0 T} \|u^0\|_{E_0} \leq S + 1, \]
and (25) and (37) ensure for $\tilde{u}_1, \tilde{u}_2 \in X_T$ and $t \in J_T$
\[ \|\Lambda(\tilde{u}_1)(t) - \Lambda(\tilde{u}_2)(t)\|_{E_0} \leq \omega_0 T \|v_{\tilde{u}_1} - v_{\tilde{u}_2}\|_{C(J_T)} \|u^0\|_{E_0} \leq \frac{1}{2} \|\tilde{u}_1 - \tilde{u}_2\|_{X_T}. \]
In order to prove that $\Lambda(\tilde{u})(t)$ is non-negative observe that $\Lambda(\tilde{u})$ also solves
\[ \dot{\tilde{u}} + (A_{\tilde{u}_a}(t) + r) u = L[u] + ru :=: B(u), \quad t > 0, \quad u(0) = u^0, \]
with $r := \|\mu + \beta\|_\infty$ and $A_{\tilde{u}_a}(t) := \tau v_{\tilde{u}_a}(t) \partial_{\tilde{u}}$. Then $B(u) \in E^+_0$ for $u \in E^+_0$. Since Lemma 2.1 ensures that $-A_{\tilde{u}_a}(s)$ generates a positive semigroup on $E_0$, it readily follows from the proof of [7, Thm.5.3.1] that the evolution system $\tilde{U}(t,s)$ generated by $\{A_{\tilde{u}_a}(t) + r\}_{t \in J_T}$ is positive. Defining then
\[ F(w)(t) := \tilde{U}(t,0) u^0 + \int_0^t \tilde{U}(t,s) B(w(s)) \, ds \]
one shows that $F$ is a contraction from a suitable closed ball in $C([0,\tilde{T}],E_0)$, containing $u^0$, into itself provided $\tilde{T} \in (0,T]$ is sufficiently small. Hence, putting
\[ u_0 := u^0, \quad u_{n+1} := F(u_n), \quad n \in \mathbb{N}, \]
we obtain a sequence in $C([0,\tilde{T}],E^+_0)$ that converges to $\Lambda(\tilde{u})|_{[0,\tilde{T}]}$. This shows that
\[ T^* := \sup\{T' \in (0,T]; \Lambda(\tilde{u})(t) \in E^+_0, 0 \leq t \leq T'\} \geq \tilde{T}. \]
Assuming $T^* < T$, a repetition of the above arguments with $u^0$ replaced by $\Lambda(\tilde{u})(T^*) \in E^+_0$ would lead to a contradiction. Thus $T^* = T$, which entails that $\Lambda : X_T \to X_T$ is indeed a contraction.
(ii) It follows from part (i) that (31), (32) admits a unique maximal solution

\[(v, u) \in C(J, \mathbb{R}^+ \times E_1^+) \cap C^1(J, \mathbb{R} \times E_0) ,\]

where \(J\) is open in \(\mathbb{R}^+\). We claim that, if \(t^+ := \sup J < \infty\), then

\[\lim_{t \nearrow t^+} v(t) = 0 \quad \text{or} \quad \lim_{t \nearrow t^+} (v(t) + \|u(t)\|_{E_1}) = \infty .\] (38)

For, suppose to the contrary that there are \(t_j \nearrow t^+ < \infty\) and \(S > 0\) such that

\[v(t_j) \geq S^{-1} \quad \text{and} \quad v(t_j) + \|u(t_j)\|_{E_1} \leq S .\]

Let \(T(S) > 0\) be the corresponding constant from part (i) and fix \(t_N > t^+ - T(S)\). Then we may choose \((v(t_N), u(t_N)) \in \mathbb{R}^+ \setminus \{0\} \times E_1^+\) as initial value and deduce that the solution \((v, u)\) can be extended to a solution on \([0, t_N + T(S)]\), contradicting its maximality.

(iii) We now show that (38) does not occur in finite time. Observe that (12) and (16) imply

\[\dot{v}(t) + \frac{d}{dt} \int_{y_0}^{\infty} y u(t, y) \, dy = \lambda - \gamma v(t) - \int_{y_0}^{\infty} y \mu(y) u(t, y) \, dy , \quad t \in J ,\] (39)

hence

\[v(t) + \|u(t)\|_{E_0} \leq v^0 + \|u^0\|_{E_0} + \lambda t , \quad t \in J .\] (40)

Suppose now that \(t^+ < \infty\). Then (40) entails that

\[\dot{v}(t) \leq \lambda + g(u(t)) \leq \lambda + \|\beta\|_{\infty} \|u(t)\|_{E_0} \leq c(t^+) , \quad t \in J ,\]

and

\[\dot{v}(t) \geq -\gamma v(t) - \tau |u(t)|_1 \quad v(t) \geq -c(t^+) , \quad t \in J .\]

Therefore

\[\|v\|_{C^1(J)} \leq c(t^+)\] (41)

and

\[v(t) \geq e^{-(\gamma+\tau|u(t)|_1) t} v^0 \geq e^{-(\gamma+\tau c(t^+)) t} v^0 > 0 , \quad t \in J .\] (42)

Taking (24) into account, we derive from (41), (42) that the evolution system

\[U_v(t, s) \text{ satisfies} \]

\[\|U_v(t, s)\|_{L(E_1)} \leq c(t^+) , \quad 0 \leq s \leq t < t^+ .\]

But then

\[\|u(t)\|_{E_1} = \|U_v(t, 0)u^0\|_{E_1} \leq c(t^+) \|u^0\|_{E_1} , \quad t \in J ,\] (43)

thus (38) cannot be true in view of (41) - (43). This contradiction proves that the solution \((v, u)\) exists for all times, hence the assertion follows. \(\square\)

If \((v, u)\) denotes the solution to (1)-(4) provided by Theorem 3.1, the next proposition shows that \(u\) propagates with finite speed. The proof is adapted from the proof of [5, Thm.2.6].

**Proposition 3.2.** Suppose (10)-(13) hold. For \(v^0 > 0\) and \(v^0 \in E_1^+\) let \((v, u)\) denote the unique global classical solution to (1)-(4). If \(\text{supp } u^0 \subset [y_0, S_0]\) for some \(S_0 > y_0\), then \(\text{supp } u(t) \subset [y_0, S(t)]\), \(t \geq 0\), where

\[S(t) := S_0 + \tau \int_0^t v(s) \, ds , \quad t \geq 0 .\]
Proof. Define \( P \in C^1(\mathbb{R}^+, L_1(Y)) \) by
\[
P(t, y) := \int_y^\infty u(t, y') \, dy' , \quad y \in Y , \quad t \geq 0 .
\]

Then, since
\[
\frac{d}{dt} P(t, y) = \int_y^\infty \dot{y} u(t, y') \, dy' = \tau v(t) u(t, y) + \int_y^\infty L[u(t)](y') \, dy',
\]
we derive from (2) and (14)
\[
\frac{d}{dt} \int_{S(t)} P(t, y) \, dy = \int_{S(t)} \frac{d}{dt} P(t, y) \, dy = S'(t) P(t, S(t))
\]
\[
= \int_S \int_y^\infty L[u(t)](y') \, dy' \, dy
\]
\[
\leq 2 \int_S \int_y^\infty \beta(y'' \kappa(y', y'') u(t, y'') \, dy'' \, dy' \, dy
\]
\[
= 2 \int_S \int_y^\infty \beta(y'') \, u(t, y'') \int_y^y \kappa(y', y'') \, dy' \, dy'' \, dy
\]
\[
\leq 2 \|\beta\|_{\infty} \int_S P(t, y) \, dy,
\]
which implies
\[
\int_{S(t)} P(t, y) \, dy \leq e^{2\|\beta\|_{\infty} t} \int_{S(0)} \int_y^\infty u^0(y') \, dy' \, dy = 0 , \quad t \geq 0 .
\]
Hence \( u(t, y) = 0 \) for \( y \in (S(t), \infty) \) and \( t \geq 0 \). \( \square \)

Remark 3.3. Note that if \( \mu(y) \geq \mu > 0 \) for a.e. \( y \in Y \) and \( \gamma > 0 \), then (39) entails
\[
v(t) + \int_0^t y \, u(t, y) \, dy \leq \frac{\lambda}{\nu} + e^{-\nu t} \left( v^0 + \|u^0\|_{\mathcal{E}_0} - \frac{\lambda}{\nu} \right) , \quad t \geq 0 , \quad (44)
\]
where \( \nu := \min\{\mu, \gamma\} > 0 \). In particular,
\[
\int_0^t v(s) \, ds \leq \frac{\lambda t}{\nu} + \frac{1}{\nu} \left( 1 - e^{-\nu t} \right) \left( v^0 + \|u^0\|_{\mathcal{E}_0} - \frac{\lambda}{\nu} \right) , \quad t \geq 0 . \quad (45)
\]

4. Weak Solutions

The aim of this section is to relax condition (10) and to prove existence of weak solutions for unbounded kernels \( \mu \) and \( \beta \). More precisely, instead of (10) we assume in the following that
\[
\left\{ \begin{array}{l}
\text{there exists } \alpha \geq 1 \text{ and } \varrho \in L_\infty^+(Y) \text{ such that }
\varrho(y) \to 0 \text{ as } y \to \infty \text{ and } \mu(y) + \beta(y) \leq \varrho(y)y^\alpha, \text{ a.e. } y \in Y .
\end{array} \right. \quad (46)
\]
In addition, we require that

\[
\sup_{|\varepsilon| \leq \delta} \frac{\beta(y)}{y^\alpha} \int_{y_0}^{y} \chi_\varepsilon(y') \kappa(y', y) \, dy' \leq \varepsilon, \quad \text{a.e. } y \in Y, \tag{47}
\]

the supremum being taken over all measurable subsets $\mathcal{E}$ in $Y$ with measure $|\mathcal{E}| \leq \delta$. Observe that (46), (47) in particular hold for kernels of the form (5) (with $\alpha > 1$). In the following we denote by $L_{1, w}(Y)$ the space $L_1(Y)$ equipped with its weak topology.

**Definition 4.1.** Given $v^0 > 0$ and $u^0 \in L_1^+(Y, y \, dy)$, we call $(v, u)$ a (global) weak solution to (1)-(4) if

(i) $g(u) \in C(\mathbb{R}^+)$,

(ii) $v \in C^1(\mathbb{R}^+) \text{ is a non-negative solution to (1),}$

(iii) $u \in C(\mathbb{R}^+, L_{1,w}(Y)) \cap L_{\infty, loc}(\mathbb{R}^+, L_1^+(Y, y \, dy))$,

(iv) for all $t > 0$ and $\varphi \in W_1^\infty(Y)$ it holds that $L[u] \in L_1((0,t) \times Y)$ and

\[
\int_{y_0}^{\infty} \varphi(y) u(t, y) \, dy - \tau \int_{0}^{t} v(s) \left( \int_{y_0}^{\infty} \varphi'(y) u(s, y) \, dy \right) ds = \int_{y_0}^{\infty} \varphi(y) u^0(y) \, dy + \int_{0}^{t} \int_{y_0}^{\infty} \varphi(y) L[u(s)](y) \, dy \, ds.
\]

We first need the following auxiliary result.

**Lemma 4.2.** Suppose that $h_n$ and $h$ are measurable functions on $Y$ such that $h_n \to h$ a.e. and let $u_n \to u$ in $L_{1,w}^+(Y)$.

(i) If $\|h_n\|_{\infty} \leq c$, then $h_n u_n \to hu$ in $L_{1,w}(Y)$.

(ii) If $g$ and $\alpha$ are as in (46) and if $|h_n(y)| \leq g(y) y^\alpha$ for a.e. $y \in Y$ and

\[
\int_{y_0}^{\infty} y^\alpha u_n(y) \, dy \leq c, \quad n \in \mathbb{N},
\]

then $h_n u_n \to hu$ in $L_{1,w}(Y)$.

**Proof.** In case that $Y$ is a finite interval, a proof of (i) is implicitly contained in [10, Lem.4.1] (a detailed proof can also be found in [12, App.]). The case of unbounded $Y$ is a slight modification thereof. Statement (ii) can be shown along the lines of [6, App.A, Cor.4.1]. Nevertheless, for the reader’s convenience, we include here a proof. First note that the assumptions imply $|h(y)| \leq g(y) y^\alpha$, a.e. $y \in Y$, and

\[
\int_{y_0}^{\infty} y^\alpha u(y) \, dy \leq c.
\]

Putting $\bar{u}_n(y) := g(y) y^\alpha u_n(y)$ and $\bar{u}(y) := g(y) y^\alpha u(y)$ we obtain for $\varphi \in L_\infty(Y)$ and $R > y_0$

\[
\left| \int_{y_0}^{\infty} \varphi(y) \left( \bar{u}_n(y) - \bar{u}(y) \right) \, dy \right| \leq \int_{y_0}^{R} \varphi(y) g(y) y^\alpha \left( u_n(y) - u(y) \right) \, dy + 2 c \|\varphi\|_{\infty} \|g\|_{L_\infty(R, \infty)}.
\]

Taking first the lim sup as $n \to \infty$ on both sides and letting then $R \to \infty$, we conclude from (46) that $\bar{u}_n \to \bar{u}$ in $L_{1,w}(Y)$. Therefore, it follows from (i) that the
right hand side of the estimate
\[
\left| \int_{y_0}^{\infty} \varphi(y) \left( h_n(y) u_n(y) - h(y) u(y) \right) dy \right|
\leq \left| \int_{y_0}^{\infty} \varphi(y) \left( \varphi(y)^{y^n} \right)^{-1} \left( h_n(y) - h(y) \right) \bar{u}_n(y) dy \right|
+ \left| \int_{y_0}^{\infty} \varphi(y) \left( \varphi(y)^{y^n} \right)^{-1} h(y) \left( \bar{u}_n(y) - \bar{u}(y) \right) dy \right|
\]
converges to 0, leading to the assertion. \qed

Now we are in a position to relax the boundedness assumptions on \( \mu \) and \( \beta \) and also the assumption on \( u_0 \) can be weakened.

**Theorem 4.3.** Suppose that (11)-(13) and (46), (47) hold. Then, given any \( \nu^0 > 0 \) and \( u^0 \in L^1_+(Y, y^\alpha dy) \), problem (1)-(4) admits at least one global weak solution \((\nu, u)\). In addition, \( u \) belongs to \( L^\infty_{\text{loc}}(\mathbb{R}^+, L^1_+(Y, y^\alpha dy)) \).

**Proof.** (i) Let \( u^0_n \in D^+(Y) \) be such that \( u^0_n \to u^0 \) in \( L^1_+(Y, y^\alpha dy) \). We define \( \mu_n := \min\{\mu, n\} \) and \( \beta_n := \min\{\beta, n\} \). Observe that \( \mu_n, \beta_n \) also satisfy (46) and (47). Then Theorem 3.1 guarantees the existence of \((\nu_n, u_n) \in C(\mathbb{R}^+, \mathbb{R}^+ \times E_1^+) \cap C^1(\mathbb{R}^+, \mathbb{R} \times E_0) \) satisfying
\[
\dot{\nu}_n = \lambda - \gamma \nu_n - \tau \nu_n \left| u_n \right|_1 + g_n(u_n), \quad t > 0, \quad \nu_n(0) = \nu^0, \quad (48)
\]
and
\[
\partial_t u_n + \tau \nu_n(t) \partial_y u_n = L_n[u_n], \quad t > 0, \quad u_n(0) = u^0_n, \quad (49)
\]
where
\[
g_n(u) := 2 \int_{y_0}^{\infty} u(y) \beta_n(y) \int_{y_0}^{y} y' \kappa(y', y) \ dy' \ dy
\]
and
\[
L_n[u](y) := - \left( \mu_n(y) + \beta_n(y) \right) u(y) + 2 \int_{y}^{\infty} \beta_n(y') \kappa(y, y') u(y') \ dy'.
\]
Let \( T > 0 \) be arbitrary. According to (40) there exists \( c_0(T) > 0 \) independent of \( n \geq 1 \) such that
\[
|v_n(t) + \|u_n(t)\|_{E_0} \leq c_0(T), \quad t \in J_T, \quad n \geq 1. \quad (50)
\]
Moreover, we claim that
\[
\|u_n(t)\|_{L^1_+(Y, y^\alpha dy)} \leq c_0(T), \quad t \in J_T, \quad n \geq 1. \quad (51)
\]
For, recall that $u_n(t)$ has compact support due to Proposition 3.2. Hence, we may test (49) by $y^\alpha$ and obtain
\[
\frac{d}{dt} \int_{y_0}^{\infty} y^\alpha u_n(t,y) \, dy = \alpha \tau v_n(t) \int_{y_0}^{\infty} y^{\alpha-1} u_n(t,y) \, dy \\
- \int_{y_0}^{\infty} y^\alpha (\mu_n(y) + \beta_n(y)) u_n(t,y) \, dy \\
+ 2 \int_{y_0}^{\infty} u_n(t,y) \beta_n(y) \int_{y_0}^{y} (y')^\alpha \kappa(y',y) \, dy' \, dy \\
\leq \alpha \tau v_n(t) \int_{y_0}^{\infty} y^{\alpha-1} u_n(t,y) \, dy
\]
for $t \geq 0$, since (12) ensures
\[
2 \int_{y_0}^{y} (y')^\alpha \kappa(y',y) \, dy' \leq y^\alpha, \quad \text{a.e. } y > y_0.
\]

Therefore, Gronwall’s inequality and estimate (50) yield (51). In particular, combining (51), (46) and (14) we deduce
\[
g_n(u_n(t)) \leq 2 y_0 \|\varrho\| \|u_n(t)\|_{L_1(Y,y^\alpha \, dy)} \leq c(T), \quad t \in J_T, \quad n \geq 1.
\]

(ii) It follows from (1) and the estimate on $g_n(u_n(t))$ that
\[
|v_n(t) - v_n(s)| \leq c(T) |t - s|, \quad t, s \in J_T, \quad n \geq 1,
\]
where $c(T) > 0$ is independent of $n \geq 1$. Taking (50) into account, the Arzelà-Ascoli theorem warrants that the sequence $(v_n)$ is relatively compact in $C(J_T)$.

(iii) We show that $(u_n)$ is relatively sequentially compact in $C(J_T, L_1(Y))$. According to a variant of the Arzelà-Ascoli theorem (see [11, Thm.1.3.2]) we merely have to check that the set \{$(u_n(t); n \geq 1)$\} is relatively compact in $L_1(Y)$ for every $t \in J_T$ and that the set \{$(u_n; n \geq 1)$\} is equicontinuous in $L_1(Y)$ at every $t \in J_T$.

First observe that (50) entails
\[
\lim_{R \to \infty} \sup_{n \geq 1} \int_{R}^{\infty} u_n(t,y) \, dy = 0. \tag{52}
\]

Let $U_{v_n}(t,s)$ denote the evolution system in $L_1(Y)$ corresponding to the operator $A_{v_n}(t) := \tau v_n(t) \partial_y$. Then
\[
\frac{\partial}{\partial t} U_{v_n}(t,0) u_n^0 + \int_{0}^{t} U_{v_n}(t,s) \frac{\partial}{\partial s} u_n[s] \, ds, \quad t \in J_T.
\]

Consequently, given $\delta > 0$, Lemma 2.4 and the positivity of $u_n(t)$ imply that
\[
\sup_{|\xi| \leq \delta} \int_{E} u_n(t,y) \, dy \leq \sup_{|\xi| \leq \delta} \int_{E} u_n^0(y) \, dy \\
+ 2 \int_{0}^{t} \sup_{|\xi| \leq \delta} \int_{y_0}^{\infty} u_n(s,y) \beta_n(y) \int_{y_0}^{y} \chi_E(y') \kappa(y',y) \, dy' \, dy \, ds.
\]
Now let $\phi$ hence derive that

From (50), (52), (53) and the Dunford-Pettis theorem (cf. [2, Thm.4.21.2]) we hence derive that $\{u_n(t); t \in J_T, n \geq 1\}$ is relatively compact in $L_{1,\infty}(Y)$. Now let $\varphi \in \mathcal{D}(Y)$ be arbitrary. Testing (49) by $\varphi$, we infer

$$\left| \int_{y_0}^{\infty} \varphi(y) [u_n(t,y) - u_n(s,y)] \, dy \right| \leq \tau \int_s^t v_n(\sigma) \int_{y_0}^{\infty} |\varphi(y)| u_n(\sigma, y) \, dy \, d\sigma$$

$$+ \int_s^t \int_{y_0}^{\infty} \varphi(y) \left( (\mu_n(y) + \beta_n(y)) u_n(\sigma, y) \right) \, dy \, d\sigma$$

$$+ 2 \int_s^t \int_{y_0}^{\infty} u_n(\sigma, y) \beta_n(y) \int_{y_0}^{y} |\varphi(y')| \kappa(y', y) \, dy' \, dy \, d\sigma$$

for $0 \leq s \leq t \leq T$, whence, from (14), (46), (50) and (51),

$$\left| \int_{y_0}^{\infty} \varphi(y) [u_n(t,y) - u_n(s,y)] \, dy \right| \leq c(T, \varphi) |t - s|, \quad t, s \in J_T. \quad (54)$$

For $\varphi \in L_{\infty}(Y)$ let $\varphi_j \in \mathcal{D}(Y)$ be such that $\varphi_j \rightarrow \varphi$ a.e. and $\|\varphi_j\|_{\infty} \leq \|\varphi\|_{\infty}$ (see [1, p.131f]). Given $\varepsilon > 0$ it follows from (52), from the fact that $\{u_n(t); t \in J_T, n \geq 1\}$ is relatively compact in $L_{1,w}(Y)$, and from Egorov’s theorem that there are $R \geq y_0$, a measurable subset $\mathcal{E}$ of $(y_0, R)$ and $j \in \mathbb{N}$ such that

$$\int_R^{\infty} u_n(t,y) \, dy + \int_\mathcal{E} u_n(t,y) \, dy \leq \frac{\varepsilon}{12 \|\varphi\|_{\infty}}, \quad t \in J_T, \quad n \geq 1,$$

and

$$\|\varphi - \varphi_j\|_{L_{\infty}((y_0, R) \setminus \mathcal{E})} \leq \frac{\varepsilon}{6 c_0(T)},$$

where $c_0(T) > 0$ stems from (50). Therefore, (54) yields

$$\left| \int_{y_0}^{\infty} \varphi(y) [u_n(t,y) - u_n(s,y)] \, dy \right| \leq \|\varphi - \varphi_j\|_{L_{\infty}((y_0, R) \setminus \mathcal{E})} \left( |u_n(t)|_1 + |u_n(s)|_1 \right)$$

$$+ \left( \|\varphi\|_{\infty} + \|\varphi_j\|_{\infty} \right) \int_\mathcal{E} (u_n(t,y) + u_n(s,y)) \, dy$$

$$+ \left( \|\varphi\|_{\infty} + \|\varphi_j\|_{\infty} \right) \int_R^{\infty} (u_n(t,y) + u_n(s,y)) \, dy$$

$$+ c(T, \varphi_j) |t - s|$$

$$\leq \varepsilon + c(T, \varphi_j) |t - s|$$

for $t, s \in J_T$ and $n \geq 1$. We conclude

$$\lim_{s \rightarrow t} \sup_{n \geq 1} \left| \int_{y_0}^{\infty} \varphi(y) [u_n(t,y) - u_n(s,y)] \, dy \right| = 0,$$

hence $\{u_n; n \geq 1\}$ is equicontinuous in $L_{1,w}(Y)$ at every $t \in J_T$. 

Since $u_n^0 \rightarrow u^0$ in $L_1(Y, y^0 \, dy)$ and in view of (47) and (51), we conclude that

$$\lim_{|E| \rightarrow 0} \sup_{n \geq 1} \int_{E} u_n(t, y) \, dy = 0. \quad (53)$$
Moreover, writing

$$u$$

in particular, we have

$$T > v, u$$

(iv) Since now $$(v_n, u_n)$$ is relatively weakly compact in $$C(J_T, \mathbb{R} \times L_{1, w}(Y))$$ for each $$T > 0$$, we may choose a subsequence (again denoted by $$((v_n, u_n))_{n \in \mathbb{N}}$$) and a function $$(v, u) \in C(\mathbb{R}^+, \mathbb{R} \times L_{1, w}(Y))$$ such that

$$(v_n, u_n) \to (v, u) \quad \text{in} \quad C(J_T, \mathbb{R} \times L_{1, w}(Y))$$

(55)

for each $$T > 0$$.

(v) We then claim that $$(v, u)$$ is a weak solution to (1)-(4). Evidently, it holds that $$(v(t), u(t)) \in \mathbb{R}^+ \times L^+_1(Y)$$ for $$t > 0$$ since $$(v_n(t), u_n(t)) \in \mathbb{R}^+ \times L^+_1(Y)$$. We fix again $$T > 0$$. Then (55) and (51) imply

$$\|u(t)\|_{L_1(Y, y^\alpha dy)} \leq c_0(T), \quad t \in J_T,$$

(56)
in particular, we have $$u \in L_{\infty, loc}(\mathbb{R}^+L_1(Y, y^\alpha dy))$$. Let $$\varphi \in W^1_{\infty}(Y)$$ be arbitrary. Clearly, (55) yields

$$\lim_{n \to \infty} \int_{y_0}^{y} \varphi(y) u_n(t, y) dy = \int_{y_0}^{y} \varphi(y) u(t, y) dy, \quad t \in J_T.$$  

(57)

Moreover, writing

$$\left| \int_0^t v(s) \int_{y_0}^{\infty} \varphi'(y) u(s, y) dy ds - \int_0^t v_n(s) \int_{y_0}^{\infty} \varphi'(y) u_n(s, y) dy ds \right|$$

$$\leq \int_0^t |v(s) - v_n(s)| \int_{y_0}^{\infty} |\varphi'(y)| u(s, y) dy ds$$

$$+ \int_0^t v_n(s) \left| \int_{y_0}^{\infty} \varphi'(y) \left[ u(s, y) - u_n(s, y) \right] \right| dy ds$$

for $$t \in J_T$$, we infer from (55), (50) and Lebesgue’s theorem that, for $$t \in J_T$$,

$$\lim_{n \to \infty} \int_0^t v_n(s) \int_{y_0}^{\infty} \varphi'(y) u_n(s, y) dy ds = \int_0^t v(s) \int_{y_0}^{\infty} \varphi'(y) u(s, y) dy ds.$$  

(58)

In addition, since $$\mu_n(y) + \beta_n(y) \leq \phi(y)y^\alpha$$ for a.e. $$y \in Y$$, we conclude from Lemma 4.2(ii), (51), (55) and Lebesgue’s theorem that

$$\lim_{n \to \infty} \int_0^t \int_{y_0}^{\infty} \varphi(y) \left( \mu_n(y) + \beta_n(y) \right) u_n(s, y) dy ds$$

$$= \int_0^t \int_{y_0}^{\infty} \varphi(y) \left( \mu(y) + \beta(y) \right) u(s, y) dy ds$$

as well as

$$\lim_{n \to \infty} \int_0^t \int_{y_0}^{\infty} \varphi(y) \int_y^{\infty} u_n(s, y') \beta_n(y') \kappa(y, y') dy' dy ds$$

$$= \int_0^t \int_{y_0}^{\infty} \varphi(y) \int_y^{\infty} u(s, y') \beta(y') \kappa(y, y') dy' dy ds,$$

where we use Fubini’s theorem for the second limit. Therefore,

$$\lim_{n \to \infty} \int_0^t \int_{y_0}^{\infty} \varphi(y) L_n[u_n(s)] dy ds = \int_0^t \int_{y_0}^{\infty} \varphi(y) L[u(s)] dy ds.$$  

(59)
Now, since \((v_n, u_n)\) is a weak solution to (1)-(4), we derive from (57)-(59) that \(u\) indeed satisfies part (iv) of Definition 4.1. Next, it follows from Lemma 4.2(ii), similarly as above, that 
\[
\lim_{n \to \infty} g_n(u_n(t)) = g(u(t)) , \quad t \in J_T ,
\]
and also 
\[
\lim_{n \to \infty} \int_0^t |u_n(s)|_1 \, ds = \int_0^t |u(s)|_1 \, ds , \quad t \in J_T .
\]
Consequently, (48) yields 
\[
v(t) = e^{-\gamma t - \tau \int_0^t |u(\sigma)|_1 \, d\sigma} v^0 + \int_0^t e^{-(\gamma(t-s) - \tau \int_s^t |u(\sigma)|_1 \, d\sigma} \left(\lambda + g(u(s))\right) \, ds
\]
for \(t \in J_T\). But since \(u \in C(\mathbb{R}^+, L_{1,w}(Y))\), Lemma 4.2(ii) and (56) warrant that \(g(u) \in C(J_T)\). In addition, \(|u|_1 \in C(J_T)\), so we deduce that \(v \in C^1(J_T)\) solves (1).

This proves the theorem.

Also the weak solution propagates with finite speed as shown in the next corollary.

**Corollary 4.4.** Suppose (11)-(13), (46), (47). If \(v^0 > 0\) and if \(u^0 \in L_1^+(Y, y^\alpha \, dy)\) is such that \(\text{supp} \, u^0 \subset [y_0, S_0]\), then the weak solution \((v, u)\) provided by Theorem 4.3 satisfies \(\text{supp} \, u(t) \subset [y_0, S(t)]\) for \(t \geq 0\), where 
\[
S(t) := S_0 + \tau \int_0^t v(s) \, ds , \quad t \geq 0 .
\]

**Proof.** We may choose the sequence \((u_n^0) \subset D^+(Y)\) in the proof of Theorem 4.3 such that \(\text{supp} \, u_n^0 \subset (y_0, S_0)\). Then Proposition 3.2 ensures that the approximating sequence \(((v_n, u_n))_{n \in \mathbb{N}}\) given in (48), (49) satisfies \(\text{supp} \, u_n(t) \subset [y_0, S_n(t)]\) for \(t \geq 0\), where 
\[
S_n(t) := S_0 + \tau \int_0^t v_n(s) \, ds , \quad t \geq 0 , \quad n \geq 1 .
\]
Evidently, \(\lim_{n \to \infty} S_n(t) = S(t)\) and 
\[
\int_{S(t)}^\infty u(t, y) \, dy = \lim_{n \to \infty} \int_{S_n(t)}^\infty u_n(t, y) \, dy = 0
\]
by (55) and Lemma 4.2(i), thus \(\text{supp} \, u(t) \subset [y_0, S(t)]\) for \(t \geq 0\). □

**Remark 4.5.** In addition to (11)-(13), (46), (47) suppose that \(\mu(y) \geq \mu > 0\) for a.e. \(y \in Y\) and that \(\gamma > 0\). Then the weak solution \((v, u)\) also satisfies the estimates (44) and (45). Indeed, (44) follows immediately from the corresponding estimate for \((v_n, u_n)\) and (55).
5. Stability of the Disease Free Steady State

This section is devoted to the investigation of the disease free steady state \((v, u) = (\lambda/\gamma, 0)\) of (1),(2). As already mentioned in the introduction it has been shown in [4] that, assuming the kernels to be of form (5), the corresponding steady state for the ordinary differential equations (6)-(8) is globally stable provided inequality (9) holds. In addition, as proven in [8], this choice of kernels leads to stability of the disease free steady state for the pde-problem. We now extend these results in that a wider class of kernels can be considered.

In the sequel, we always assume that (11)-(13) are satisfied with \(\gamma > 0\) and that either
\[
\begin{cases}
(10) & \text{holds}, \\
v^0 > 0, \quad u^0 \in E^+_1,
\end{cases}
\]

or
\[
\begin{cases}
(46), (47) & \text{hold}, \\
v^0 > 0, \quad u^0 \in L^+_1(Y, y^\alpha dy).
\end{cases}
\]

Then we denote by \((v, u)\) either the classical solution provided by Theorem 3.1 if (60) holds, or the weak solution provided by Theorem 4.3 if (61) holds.

We introduce \(\mu, \varepsilon_k, \delta_k\) such that
\[
0 \leq \mu \leq \mu(y), \quad \text{a.e. } y \in Y,
\]
and
\[
0 \leq \delta_k \leq \beta(y) \int_0^{y_0} (y')^k \kappa(y', y) dy' \leq \varepsilon_k, \quad \text{a.e. } y \in Y,
\]
for \(k = 0, 1\), assuming at least \(\varepsilon_1\) to be finite. Moreover, we put
\[
B := 2 \delta_1 - \varepsilon_1 - \frac{\tau \lambda^2}{2\gamma},
\]
and, for \(b > 0\),
\[
C(b) := b (\mu + 2 \delta_0) + 4 \lambda \delta_1 \gamma \left[ \frac{\tau \lambda^2}{2\gamma} - \frac{2 \varepsilon_1^2}{\tau} - \frac{2 \lambda \varepsilon_1}{\gamma} \right]
\]
as well as
\[
D(b) := B^2 + \frac{\tau}{2} C(b) = \frac{b \tau}{2} (\mu + 2 \delta_0) - 4 \delta_1 (\varepsilon_1 - \delta_1).
\]

**Lemma 5.1.** Suppose (60) or (61) holds and that there are constants \(b > 0\) and \(q \geq 0\) such that
\[
(i) \quad D(b) > 0,
\]
\[
(ii) \quad a^*_+ > 0 \quad \text{for} \quad a^*_+ := \frac{4}{\tau} \left( B \pm \sqrt{D(b)} \right),
\]
\[
(iii) \quad \text{there exists} \quad a \in \left( \min \{ 0, a^*_+ \}, a^*_+ \right) \text{ with}
\]
\[
\frac{\beta(y)}{y} \leq \frac{a}{b} \mu(y) - \frac{q}{b}, \quad \text{a.e. } y \in Y.
\]

Then \(p := -\frac{\tau}{8} a^2 + B a + C(b) > 0\) and for
\[
F(v, u) := \left( v - \frac{\lambda}{\gamma} \right)^2 + a \int_{y_0}^\infty y u(y) dy + b \int_{y_0}^\infty u(y) dy
\]
it holds that
\[
F(v, u)(t) + p \int_0^t \int_{y_0}^{\infty} u(s, y) \, dy \, ds + q \int_0^t \int_{y_0}^{\infty} y u(s, y) \, dy \, ds \leq F(v^0, u^0)
\]
for each \( t \geq 0 \), where \((v, u)\) is either the classical solution or the weak solution constructed in Theorem 3.1 or Theorem 4.3, respectively.

Proof. Since in the case of the classical solution one can show directly that
\[
\frac{d}{dt} F(v, u)(t) \leq -p |u(t)|_1 - q \int_{y_0}^{\infty} u(t, y) \, dy , \quad t \geq 0 ,
\]
using estimates very close to the subsequent ones, we will focus on the case of weak solutions. Therefore, let \((v_n, u_n)\) be the approximations of \((v, u)\) corresponding to the data \((v^0, u_n^0, \beta_n, \mu_n)\) as in the proof of Theorem 4.3. Then it follows from (12), (14) and (16) that
\[
\frac{d}{dt} F(v_n, u_n)(t) = -2 \gamma \left( v_n - \frac{\lambda}{2} \right)^2 - 2 \tau v_n^2 |u_n|_1 + \frac{2 \tau \lambda}{\gamma} v_n |u_n|_1 + 4 \left( v_n - \frac{\lambda}{\gamma} \right) \int_{y_0}^{\infty} u_n(y) \beta_n(y) \left[ \int_0^{y_0} y' \kappa(y', y) \, dy' \right] \, dy + a \int_{y_0}^{\infty} \mu_n(y) u_n(y) \, dy \\
- 2 a \int_{y_0}^{\infty} u_n(y) \beta_n(y) \left[ \int_0^{y_0} y' \kappa(y', y) \, dy' \right] \, dy - b \int_{y_0}^{\infty} \mu_n(y) u_n(y) \, dy \\
+ b \int_{y_0}^{\infty} u_n(y) \beta_n(y) \left( 1 - 2 \int_0^{y_0} \kappa(y', y) \, dy' \right) \, dy .
\]
Recalling that \( \mu \geq 0 \) and \( \varepsilon_1 < \infty \), integration of the above equality yields (for \( n > \mu \))
\[
F(v_n, u_n)(t) + \int_0^t |u_n(s)|_1 \left( 2 \tau v_n(s)^2 + b \mu \right) \, ds \\
+ \int_0^t \int_{y_0}^{\infty} u_n(s, y) \beta_n(y) \left[ \left( \frac{4 \lambda}{\gamma} + 2 a \right) \int_0^{y_0} \kappa(y', y) \, dy' \right] \, dy \\
+ b \int_0^t \int_{y_0}^{\infty} y' \kappa(y', y) \, dy' \, ds \\
+ a \int_0^t \int_{y_0}^{\infty} \mu_n(y) u_n(s, y) \, dy \, ds \\
\leq F(v^0, u_n^0) + b \int_0^t \int_{y_0}^{\infty} u_n(s, y) \beta_n(y) \, dy \, ds \\
+ \int_0^t |u_n(s)|_1 v_n(s) \, ds \left( \frac{2 \tau \lambda}{\gamma} + a \tau + 4 \varepsilon_1 \right) .
\]
Observe then that \((55)\) ensures
\[
F(v, u)(t) \leq \lim_{n \to \infty} F(v_n, u_n)(t), \quad t \geq 0.
\] (63)

Next, \((55)\) and Lebesgue’s theorem imply
\[
\lim_{n \to \infty} \int_0^t |u_n(s)|_1 v_n(s) \, ds = \int_0^t |u(s)|_1 v(s) \, ds, \quad t \geq 0.
\] (64)

As in \((59)\) one shows that
\[
\lim_{n \to \infty} \int_0^t \int_{y_0}^\infty \chi_{(y_0, R)}(y) u_n(s, y) \mu_n(y) \, dy \, ds
= \int_0^t \int_{y_0}^\infty \chi_{(y_0, R)}(y) u(s, y) \mu(y) \, dy \, ds
\]
for \(k = 0, 1\). Owing to Lemma 4.2, \((46)\), \((50)\) and \((55)\) we may apply Lebesgue’s theorem to conclude
\[
\lim_{n \to \infty} \int_0^t \int_{y_0}^\infty \chi_{(y_0, R)}(y) u_n(s, y) \beta_n(y) \, dy \, ds
= \int_0^t \int_{y_0}^\infty \chi_{(y_0, R)}(y) u(s, y) \beta(y) \, dy \, ds
\]
for each \(R > y_0\), hence
\[
\int_0^t \int_{y_0}^\infty u(s, y) \mu(y) \, dy \, ds \leq \lim_{n \to \infty} \int_0^t \int_{y_0}^\infty u_n(s, y) \mu_n(y) \, dy \, ds.
\] (66)

Thus, in view of \((63)-(66)\) we may pass to the limit in \((62)\) to deduce that this inequality is still true if we replace \((v_n, u_n)\) by \((v, u)\) and \((\beta_n, \mu_n)\) by \((\beta, \mu)\), respectively. Rearranging the terms and using the definition of \(\delta_k\) we derive
\[
F(v, u)(t) + \int_0^t |u(s)|_1 \left[ 2\tau v(s)^2 - \left( \frac{2\tau \lambda}{\gamma} + 4\varepsilon_1 + a\tau \right) v(s) \right. \\
+ b(\mu + 2\delta_0) + \left( \frac{4\lambda}{\gamma} + 2a \right) \delta_1 \] \hspace{1cm} ds
+ \int_0^t \int_{y_0}^\infty (a y \mu(y) - b \beta(y)) u(s, y) \, dy \, ds
\leq F(v^0, u^0)
\]
for each \(t \geq 0\). Observing that \(p > 0\) is a lower bound for what is inside the brackets by assumption (ii), the assertion is a consequence of assumption (iii).

The next theorem shows that the disease free steady state is asymptotically stable.

**Theorem 5.2.** Suppose \((60)\) or \((61)\) is satisfied and (i)-(iii) of Lemma 5.1 hold. Then, given \(\varepsilon > 0\) there exists \(\delta > 0\) such that
\[
|v(t) - \lambda/\gamma| + \|u(t)\|_{E_0} \leq \varepsilon, \quad t \geq 0,
\]
whenever
\[
|v^0 - \lambda/\gamma| + \|u^0\|_{E_0} \leq \delta,
\]
where \((v, u)\) is either the classical solution or the weak solution constructed in **Theorem 3.1** or **Theorem 4.3**, respectively.
Moreover, if \( \beta(y) \leq B y \) for a.e. \( y \in Y \) and some \( B > 0 \), then
\[
(v(t), u(t)) \longrightarrow 0 \quad \text{in} \quad \mathbb{R} \times L_1(Y, y^\gamma \mathrm{d}y) \quad \text{as} \quad t \longrightarrow \infty
\]
for each \( \sigma < 1 \).

**Proof.** The first statement readily follows from the fact that \( F(v, u)(t) \leq F(v^0, u^0) \) for \( t \geq 0 \). Next, Lemma 5.1 ensures that
\[
\|u(t)\|_{L_1(Y, y^\sigma \mathrm{d}y)} \leq \frac{1}{a} F(v^0, u^0), \quad t \geq 0. \tag{67}
\]
Furthermore, by definition of a weak solution we have
\[
|u(t)|_1 = |u^0|_1 + \int_0^t \int_{y_0}^\infty L[u(s)](y) \mathrm{d}y \mathrm{d}s, \quad t \geq 0,
\]
from which we infer that
\[
\frac{1}{h} \left( |u(t+h)|_1 - |u(t)|_1 \right) = \frac{1}{h} \int_t^{t+h} \int_{y_0}^\infty L[u(s)](y) \mathrm{d}y \mathrm{d}s \\
\leq \frac{1}{h} \int_t^{t+h} \int_{y_0}^\infty u(s,y) \beta(y) \mathrm{d}y \mathrm{d}s \\
\leq B \sup_{s \geq 0} \|u(s)\|_{L_1(Y, y^\sigma \mathrm{d}y)},
\]
for \( t \geq 0 \) and \( h > 0 \). Thus, (67) yields
\[
|u(t+h)|_1 - |u(t)|_1 \leq c h, \quad t, h > 0. \tag{68}
\]
Lemma 5.1 also ensures that
\[
\int_0^\infty |u(s)|_1 \mathrm{d}s \leq \frac{1}{p} F(v^0, u^0). \tag{69}
\]
Combining (68) and (69) we conclude that \( \lim_{t \to \infty} |u(t)|_1 = 0 \), which, together with (67), warrants that for each \( \sigma < 1 \)
\[
u(t) \longrightarrow 0 \quad \text{in} \quad L_1(Y, y^\sigma \mathrm{d}y) \quad \text{as} \quad t \longrightarrow \infty. \tag{70}
\]
Finally, since \( \varepsilon_1 < \infty \) both \( g(u(t)) \) and \( |u(t)|_1 \) tend to 0 as \( t \to \infty \) due to (70). Since \( v \in C^1(\mathbb{R}^+) \) solves (1), it is easy to check that \( v(t) \) converges to \( \lambda/\gamma \). \( \square \)

**Corollary 5.3.** If (60) and (i)-(iii) of Lemma 5.1 hold, then the classical solution \((v, u)\) corresponding to \( v^0 > 0 \) and \( u^0 \in E_1^+ \) satisfies
\[
(v, u) \longrightarrow (\lambda/\gamma, 0) \quad \text{in} \quad \mathbb{R} \times L_1(Y, y^\sigma \mathrm{d}y) \quad \text{as} \quad t \longrightarrow \infty
\]
for each \( \sigma < 1 \). Moreover, if also \( q > 0 \) in Lemma 5.1, then
\[
u \longrightarrow 0 \quad \text{in} \quad L_1(Y, y^\sigma \mathrm{d}y) \quad \text{as} \quad t \longrightarrow \infty.
\]

**Proof.** The first statement is due to Theorem 5.2. Next, set
\[
Q(t) := \int_{y_0}^\infty y u(t,y) \mathrm{d}y \geq 0, \quad t \geq 0.
\]
Then \( Q \in C^1(\mathbb{R}^+) \) according to Theorem 3.1. If \( q > 0 \), Lemma 5.1 ensures that
\[
Q(t) + \int_0^\infty Q(s) \mathrm{d}s \leq c, \quad t \geq 0. \tag{71}
\]
In addition, \( v(t) \leq c \) for each \( t \geq 0 \), so it follows from (12), (16) and (71) that
\[
\dot{Q}(t) \leq \tau v(t)|u(t)|_1 + 2 \int_{y_0}^{\infty} u(t, y) \beta(y) \int_{y_0}^{y'} \kappa(y', y) \, dy' \, dy \leq c, \quad t \geq 0. \tag{72}
\]
Consequently, we deduce \( \lim_{t \to \infty} Q(t) = 0 \) from (71) and (72).

\[\Box\]

**Remark 5.4.** Observe that if the kernels are of the form (5), a straightforward calculation shows that assumptions (i)-(iii) of Lemma 5.1 are equivalent to (9). Therefore, given any initial value \((v^0, u^0)\) such that \( v^0 > 0 \) and \( u^0 \in L^+_1(Y, y^\alpha \, dy) \) for some \( \alpha > 1 \), the weak solution \((v, u)\) provided by Theorem 4.3 satisfies
\[
(v, u) \longrightarrow (\lambda/\gamma, 0) \quad \text{in} \quad \mathbb{R} \times L^1_1(Y, y^\sigma \, dy) \quad \text{as} \quad t \to \infty
\]
for each \( \sigma < 1 \) according to Theorem 5.2.

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**REFERENCES**


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